CLAIMS

We claim:

1. A crystallized molecule or molecular complex comprising a binding pocket defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 150, 151, 156, 160, 199, 232, 253, 254, 256, 281, 282, 283, 284, 306, 311, 312, and 317 according to Figure 1, or a homologue of said molecule or molecular complex wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

2. The crystallized molecule or molecular complex according to claim 1, wherein said binding pocket is defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 150, 151, 156, 160, 199, 281, 282, 283, 306, 311, 232, and 254, according to Figure 1, or a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

3. A crystallized molecule or molecular complex comprising a binding pocket defined by structure coordinates of CnA amino acids 122, 124, 159, 160, 310, 312, 313, 314, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and CnB amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 123, 157, 158, 159, 161, and 162 according to Figure 1, or a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

4. The crystallized molecule or molecular complex according to claim 1, further comprising a second binding

pocket defined by CnA amino acids 122, 124, 159, 160, 310, 312, 313, 314, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and CnB amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 124, 157, 158, 159, 161, and 162; according to Figure 1, or a homologue of said molecule or molecular complex, wherein said homologue comprises a second binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

5. The crystallized molecule or molecular complex according to claim 4, wherein said molecule or molecular complex is defined by the set of structure coordinates according to Figure 1, or a homologue thereof, wherein said homologue has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

6. The crystallized molecule or molecular complex according to claim 4, wherein said molecule or molecular complex comprises amino acids 17-392 of CnA, CnB, FKBP12 and FK506.

7. A machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, is capable of displaying a graphical three-dimensional representation of a molecule or molecular complex comprising a binding pocket defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 150, 151, 156, 160, 199, 232, 253, 254, 256, 281, 282, 283, 284, 306, 311, 312, and 317 according to Figure 1, or a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

8. The machine-readable storage medium according to claim 7, wherein said binding pocket is defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 150, 151, 156, 160, 199, 281, 282, 283, 306, 311, 232, and 254 according to Figure 1, or a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

9. A machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, is capable of displaying a graphical three-dimensional representation of a molecule or molecular complex comprising a binding pocket defined by structure coordinates of CnA amino acids 122, 124, 159, 160, 310, 312, 313, 314, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and CnB amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 124, 157, 158, 159, 161, and 162 or a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

10. The machine-readable storage medium according to claim 7, wherein said molecule or molecular complex further comprises a second binding pocket defined by structure coordinates of CnA amino acids 122, 124, 159, 160, 310, 312, 313, 314, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and CnB amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 124, 157, 158, 159, 161, and 162 according to Figure 1, or a homologue of said molecule or molecular complex, wherein said homologue comprises a second binding pocket

that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

11. The machine-readable data storage medium according to claim 10, wherein said molecule or molecular complex is defined by the set of structure coordinates according to Figure 1, or a homologue of said molecule or molecular complex, said homologue having a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

12. A machine-readable data storage medium comprising a data storage material encoded with a first set of machine readable data which, when combined with a second set of machine readable data, using a machine programmed with instructions for using said first set of data and said second set of data, can determine at least a portion of the structure coordinates corresponding to the second set of machine readable data, wherein:
said first set of data comprises a Fourier transform of at least a portion of the structural coordinates according to Figure 1; and said second set of data comprises an X-ray diffraction pattern of a molecule or molecular complex.

13. A method for evaluating the ability of a chemical entity to associate with a molecule or molecular complex according to any one of claims 1 to 6 comprising the steps of:

a. employing computational means to perform a fitting operation between the chemical entity and a binding pocket of the molecule or molecular complex; and

b. analyzing the results of said fitting operation to quantify the association between the chemical entity and the binding pocket.

14. A method of utilizing molecular replacement to obtain structural information about a molecule or a molecular complex comprising the steps of:

a. crystallizing said molecule or molecular complex;

b. generating an X-ray diffraction pattern from said crystallized molecule or molecular complex;

c. applying at least a portion of the structure coordinates set forth in Figure 1 to the X-ray diffraction pattern to generate a three-dimensional structure of at least a portion of the molecule or molecular complex.

15. The method according to claim 14, wherein the molecule or molecular complex comprises a polypeptide selected from a catalytically functional calcineurin A subunit.

16. A method for preparing a CnA/CnB/FKBP12/ FK506 crystal comprising the steps of:

a. forming a molecular complex between FKBP12, FK506, calcineurin A and calcineurin B, wherein the calcineurin A lacks a calmodulin binding domain and an autoinhibitory domain; and

b. crystallizing the digested complex.

17. The method according to claim 16, wherein the calmodulin binding domain and the autoinhibitory domain of said calcineurin A are removed by proteolytic digestion with a protease selected from clostripain, trypsin, endoproteinase Lys-C, endoproteinase Asp-N, endoproteinase Glu-C, elastase, enterokinase, restriction protease Factor Xa, thermolysin, Il-1 beta converting enzyme or HIV-1 protease.

18. The method according to claim 17, wherein the

protease is clostripain and the calcineurin A subunit in the crystallized complex has a molecular weight of about 42 kDa.

Add A1

add D2

ADD F3